Remarks

I. Status of Claims.

Claims 1-13 are pending.

Claims 1, 5, 7 and 13 are amended in a manner that is believed to overcome rejections contained in the pending Office Action. Claims 14-16 have been added to further emphasize Applicants' elected subject matter. Support for these newly added claims and amendments can be found throughout the drawings and specification. No new matter or issues are believed to be introduced by these amendments and newly added claims. Support for the amendments is found throughout the specification and drawings.

II. Objection to Abstract.

The Examiner objected to the abstract of the disclosure as containing more than one paragraph. Applicants' attorney, John C. Serio, conferenced this objection with the Examiner and the objection to the abstract has been withdrawn. Applicants thank the Examiner for courtesies extended in granting and conducting the conference and for his diligence in the examination of the instant application.

III. Rejection of Claims 1, 5, 7 and 13 under 35 USC 112, second paragraph.

The Examiner rejected claims 1, 5, 7 and 13 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of Applicants' invention.

The Examiner rejected claim 1 for the indefinite use of the phrase "Prodrug compounds" and suggested Applicants amend claim 1 to read in the singular form, "A prodrug compound". Applicants have amended claim 1 to reflect the Examiner's suggestion. Applicants thank the Examiner for this suggested amendment and for his diligence in the examination of the instant application. Applicants would respectfully request that this rejection be withdrawn.

The Examiner further rejected claim 1 for being drawn to non-elected subject matter. Applicants respectfully traverse this rejection.

The Examiner's current rejection that claim 1 is to unelected subject matter is improper. Per the restriction requirement of September 19, 2002, claim 1 was part of Group I, the group that was elected by Applicants in their response. As part of the restriction requirement, because claim 1 was a generic claim, Applicants as required elected a species as well. Applicants are entitled to maintain their generic claim in its current form until such time as the Examiner can substantiate a proper rejection of such claim. This has not been done. Applicants would respectfully request that this rejection be withdrawn.

The Examiner rejected claims 5, 7 and 13 for the recitation of plural "compounds" regarding the claimed product. Applicants have amended claims 5, 7 and 13 as suggested by the Examiner. Applicants thank the Examiner for his guidance.

The Examiner further rejected claim 7 under 35 USC 112, second paragraph for the recitation of the terms "optionally" and "customary" which were identified as indefinite. In accordance with the Examiner's suggestions, Applicants have amended claim 7 to remove the basis of this rejection.

The Examiner further rejected claim 13 under 35 USC 112, second paragraph for the recitation of the indefinite term "preventing." The Examiner suggested that if Applicants were to amend claim 13 to read, "inhibiting the degradation" then claim 13 would be in compliance with the requirements of 35 USC 112. Applicants have amended the claim in accordance with this suggestion.

The Examiner also further rejected claim 13 under 35 USC 112, second paragraph for the use of the term "complex." The Examiner suggested that if Applicants were to amend claim 13 to read, "composition" then claim 13 would be in compliance with the requirements of 35 USC 112. Applicants have so amended the claim and thank the Examiner for this suggestion.

As Applicants have complied with the Examiner's suggestions, they respectfully request withdrawal of the 112 rejections.

IV. Rejection of claims 1 and 7 under 35 USC 102(b).

The Examiner rejected claims 1 and 7 under 35 USC 102(b) as being anticipated by Tanaka et al. ("Tanaka"). The Examiner stated that Tanaka teaches a DP IV inhibitor of a general formula A-B-C, wherein A is an amino acid, B is a bond between A and C, and C is a

stable inhibitor of DP IV. Applicants respectfully but vigorously disagree with this evaluation of Tanaka and traverse this rejection.

Tanaka discloses the use of several DP VI inhibitors to suppress symptoms of alkyldiamine induced arthritis. Specifically, the DP IV inhibitors disclosed in Tanaka are Lys(Z(NO_2)thiazolidide and Ala-Pro-nitrobenzoylhydroxylamine. These compounds are distinct from the compounds claimed by Applicants.

To clarify, Applicants respectfully point out that the single compound groups, each represented by A, B and C, are not prodrugs per se. A is defined as an amino acid. Amino acids are not prodrugs. B is either a chemical bond between A and C or is an amino acid. As stated above, amino acids are not prodrugs. C is not merely an amino acid but rather a stable inhibitor of dipeptidyl peptidase IV activity without a C-terminal phosphonate residue. However, this stable inhibitor of dipeptidyl peptidase IV activity is also not a prodrug itself. Examples for A, B and C are listed in table 1 below.

Only the combination of all three elements, A, B and C, forms a prodrug. Indeed, the compounds A-B-C represent new chemical entities, which comprise enzyme inhibitors for DP IV with surprising and unique characteristics. To summarize, it may be stated that, by means of the prodrug compounds of DP IV-inhibitors according to the invention, it is possible, in an entirely unexpected manner:

1. to achieve increased action of the inhibitors;
2. for the inhibitors to be released according to the treated patient's needs;
3. for the inhibitors to be released from the prodrug compounds in a temporally controlled manner;
4. for the site at which the inhibitors are released from the prodrug compounds to be controlled; and
5. for a reservoir of DP IV-inhibitors to be provided.

Examples of A, B and C and their position in the prodrug compound A-B-C are given in table 1 to illustrate the present invention. Compound Pro-Ile-Thia in table 1 corresponds to the formula A-B-C as follows: Pro=A, bond=B, Ile-Thia=C.

Table 1

	A	B	C
1			Ile-Thia
2	Gly	Pro	Ile-Thia
3	Pro		Ile-Thia
4	Ile	Pro	Ile-Thia
5	Pro	Pro	Ile-Thia

Applicants respectfully point out that the Tanaka does not disclose a prodrug compound of the formula A-B-C. When compared to the prodrug compounds of the present invention, the Tanaka compounds Lys(Z(NO_2)thiazolidide and Ala-Pro-nitrobenzoylhydroxylamine represent only part C. If one were to 'break' up Tanaka's molecules in order to assign components to A, B and C, one would not have an inhibitor for part C as required by Applicants' claims. Rather, Ala-Pro-nitrobenzoylhydroxylamine falls under the group of N-dipeptidyl, O-acyl hydroxylamines, which are clearly defined as part C of the compounds of the present invention, stable inhibitors of dipeptidyl peptidase IV activity. This is supported by the specification at page 5, lines 8-11. Tanaka fails to disclose the necessary A and B components, as required by claims 1 and 7.

Applicants would therefore request that this rejection be withdrawn.

V. Rejection of claims 1 and 7 under 35 USC 102(b).

The Examiner rejected claims 1 and 7 under 35 USC 102(b) as being anticipated by Augustyns et al. ("Augustyns"). The Examiner stated that Augustyns teaches a DP IV inhibitor of a general formula A-B-C, wherein A is an amino acid, B is a bond between A and C, and C is a stable inhibitor of DP IV. Specifically, Augustyns teaches the DP IV inhibitor 1-(L-Isolucyl)-3(S)-fluoroyrrolidine. Applicants traverse this rejection.

Applicants respectfully point out that Augustyns does not disclose a prodrug compound of the formula A-B-C. As was the case with Tanaka, when compared to the prodrug compounds of the present invention, Augustyns' compound 1-(L-Isoleucyl)-3(S)-fluoropyrrolidine ,

represents only part C. Augustyns provides no components for A or B as required by claims 1 and 7 and accordingly fails to disclose prodrugs of the formula A-B-C as claimed in the present invention. Applicants therefore request that this rejection be withdrawn.

VI Rejection of claim 5 under 35 USC 103(a).

The Examiner rejected claim 5 under 35 USC 103(a) as being unpatentable over Augustyns et al. ("Augustyns"). The Examiner states that Augustyns teaches a DP IV inhibitor of a general formula A-B-C, wherein A is an amino acid, B is a bond between A and C, and C is a stable inhibitor of DP IV by providing the DP IV inhibitor 1-(L-Isoleucyl)-3(S)-fluoropyrrolidine. The Examiner acknowledges that Augustyns does not teach a salt form. Applicants traverse this rejection.

As has been earlier detailed, Augustyns utterly fails to disclose a prodrug compound of the formula A-B-C. Augustyns' compound, 1-(L-Isoleucyl)-3(S)-fluoropyrrolidine, is an inhibitor and represents only component C. If the compound is broken down to assign elements to each of A, B and C, then the element assigned to C would not be an inhibitor as required by Applicants' claim. To his inhibitor, Augustyns provides no suggestion to add additional components generally, or components A and B, specifically, to derive a compound of the formula A-B-C as set forth in claim 5. Applicants would therefore respectfully, but vigorously suggest that this rejection may be properly withdrawn.

CONCLUSION

Applicants respectfully request expeditious consideration and passage of the present application to issuance. The Examiner is invited and encouraged to telephone the undersigned if she believes such would facilitate prosecution of the present application.

Respectfully submitted,

By: _____

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